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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,403	06/04/2001	Pramod K. Srivastava	8449-178-999	1802

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,403	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-9 and 37-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7 & 12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I in Paper No. 11 is acknowledged.

2. Claims 5,6,10-29, and 30-36 are canceled without prejudice, claims 37-42 are newly added and entered into the record. Therefore, claims 1-4, 7-9, and 37-42 are pending and examined on the record.

Information Disclosure Statement

3. The Information Disclosure Statements filed 9/25/2001 and 10/23/2002 (paper no. 7 and 12) are acknowledged and considered. A signed copy of the IDS is attached hereto.

Inventorship

4. In view of the papers filed 8/13/2002, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding Arobert J. Binder to the inventorship.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 112,2nd paragraph

5. Claims 1-4, 7-9, and 37-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Regarding claim 1 and dependent claims thereof, the metes and bounds of the term "amount" cannot be determined because the actual quantity of the purified molecular complex has not been defined.

7. Regarding claim 1, 7 and dependent claims thereof, it is unclear as to which diseases are associated with the term proliferative disorders. Rheumatoid arthritis is associated with a proliferative disorder of endothelial cells, wherein there is an increase in the amount of angiogenesis, is this also encompassed by the term?

8. Regarding claim 1 and dependent claims thereof in the recitation of the term "antigen", it is unclear as to the metes and bounds of the term because it has not been adequately defined in the specification.

9. Regarding claims reciting the term "infectious agent", it is unclear as to the exact meaning of the term because the intended metes and bounds of the term have not been defined by the specification.

10. Regarding claims reciting "at least 65%" it is unclear as to how this is to be measured and what other compounds or molecules will be representing the other 35% of the purified complexes.

Claim Rejections - 35 USC § 112,1st paragraph

11. Claims 1-4, 7-9, and 37-42 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an alpha 2 macroglobulin (α2M) acting as an antagonist to HSP-antigen complexes does not reasonably provide enablement for a composition or purified α2M-peptide complex that has a non-covalently associated antigen with antigenicity of an infectious agent or of a tumor associated antigen or tumor specific antigen used for the prevention of an infectious disease or a proliferative disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent

Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a composition comprising a molecular complex of α2M with an antigenic molecule or a purified molecular complex comprising an α2M associated with an antigenic molecule, wherein the antigenic molecule is either derived from an infectious disease or from an proliferative disorder.

The amount of direction or guidance present and the presence or absence of working examples: It is the examiners understanding that the instant invention is drawn to a composition or purified complex comprising α2M peptide associated with an antigen either derived from an infectious agent or from a tumor or cancer cell, wherein the α2M peptide encompasses either the entire α2M protein or portions of the substrate binding domain of α2M. Such complex would then be able to bind to the α2M receptor and potentially compete with heat shock proteins (HSP) for binding. Because the complex is associated with an antigen, the antigen would then be process by the antigen presenting cell through a MHC I pathway, thereby eliciting an immune response to that specific antigen.

The instant specification teaches the identification of a receptor for gp96, a HSP, wherein the receptor is α2M receptor (aka LDL receptor related protein or LRP). The

specification goes into explicit detail explaining the method steps and procedures used to identify and characterize the receptor for gp96. The specification also embodies desired methods and envisions the desired products of which are claimed in the instant application. However, no wherein the specification does it teach the actual use or construction of any specific composition or the isolation of a molecular complex comprising α2M associated with an antigen derived from an infectious disease or from a cancer. Because the specification has inadequately described the composition encompassed by the claims, one of skill in the art would be forced into undue experimentation.

The skilled artisan would be forced to determine a multitude of factors and variables. Some of the factors or variables one of skill would be forced to resolve include:

(1) Determine if the desired composition or purified complex would elicit an autoimmune response. Because the modulation of the immune system is an unpredictable art, the determination of whether the introduction of the desired composition of purified complex into the a cell would indeed elicit a response directed at the antigen of choice or to a self antigen not involved in a pathological disease or a self antigen is not fully understood or clear.

(2) Determine if the α2M peptide is capable of functioning. Because the specification has not taught the actual construction of the complex either in composition form or in purified form, one of skill would need to determine if the complex is still able to function in the same manner as disclosed in the working example. The specification

teaches that the α2M peptide may consist of the substrate binding portion. If the said peptide only consists of such a portion, the α2M receptor binding domain may be missing and thereby unable to elicit the desired intended use. Such incapacity to bind may lead to antibody generation to the composition and or purified complex causing undue immune response.

(3) Determine if the antigen presented in association with α2M peptide is able to elicit an MHC I immune response. As stated above, the modulation of the immune system is an unpredicatable art. The specification alludes to the fact that gp96-peptide complex elicits an immune response through MHC I pathway thereby eliciting CD8+ cells. In some cases of disease treatment the elicitation of a MHC II type response may be more appropriate. The specification has not taught whether the complex would definitive elicit a MHC I or II response, as such the skill artisan must determine the response of the antigen before complexing with the α2M peptide.

(4) Determine which proliferative diseases are encompassed. Currently, the claims read on any and all types of proliferative diseases, ranging from cancer to hypertrophy to restenosis to benign growths. Although in theory any antigen could be used, one of skill would need to experiment to determine if antigens associated with other types of proliferative diseases can be used in the composition or purified complex of the instantly claimed invention.

(5) Determine the antigen used. Currently any and all antigens are encompassed by the claims of the instant invention. The specification has provided a laundry list of potential antigens for the skilled artisan from which to choose. However,

the specification has not taught which ones are able to be associated and elicit an immune response.

(6) How to prevent diseases such as cancer or HIV. The claims encompass disease such as cancer and HIV, wherein the instant invention allegedly is able to prevent. One of skill in the art would be forced into undue experimentation to determine how to effectively prevent such diseases. Currently, there is no means of preventing either disease because there are many factors of which there is little information or knowledge such as prescreening for patients that are predisposed to developing cancer and or the treatment of HIV. All of which the specification has provided little to no guidance so as to teach one of skill in the art how to practice such methods.

Currently, the specification has only enabled one of skill in the art to use either gp96 or α2M to antagonize each other in binding to the α2M receptor. The instant specification has not enabled a composition or a purified complex comprising a α2M peptide associated with an antigen derived from an infectious disease or a cancer cell (i.e. tumor associated antigen or tumor specific antigen).

The breadth of the claims and the quantity of experimentation needed: Given the inadequate disclosure of the composition and or purified complex, the unpredicatability of manipulating the immune system and the broad range of proliferative diseases and antigens encompassed by the claims, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1,3,4,7,8,38,39,and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Otto A *et al* (J. Urol 1998 Jan;159(1):297-303). Claims are drawn to a composition comprising a molecular complex or a purified molecular complex, wherein the molecular complex comprises α2M peptide associated with a antigen from a cell of a proliferative disorder, wherein the proliferative disorder is cancer (specifically prostate cancer) and the antigen is a tumor associated antigen or a tumor specific antigen. The claims are further drawn to a purified molecular complex wherein the complex is at least 65% of the total population is noncovalently associated. For the purposes of this rejection, the α2M peptide is interpreted to mean a full length α2M protein. Otto A *et al* teach that PSA can be associate with α2M and that between 95-99% of the complex is in non-covalent form. The composition is also anticipated because the composition is considered to be an intended usage of the basic product, which is a molecular complex comprising a α2M associated with an antigen from a cell which is involved in a proliferative disorder.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
January 27, 2003

ALI R. SALIMI
PRIMARY EXAMINER